The Genetic Testing Quality Control Materials Program (GTQC) - A Sustainable Community Process to Improve Availability of Appropriate, Verified Quality Control (QC) Materials for Genetic Testing

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The Genetic Testing Quality Control Materials Program (GTQC)

The CDC Genetic Testing Quality Control Materials Program (GTQC) was developed based on recommendations from three Quality Control Materials meetings held in September 2003, March 2004 and November 2004 (http://www.phppo.cdc.gov/mlp/qcgeneticconference/proceedings.aspx).

Background

There has been a rapid increase in the number and volume of genetic tests in the last few years. Currently, genetic testing for over 1000 diseases is performed in clinical or research settings with approximately 10 new tests being made clinically available each month. The annual volume of cystic fibrosis testing has increased significantly since preconception and prenatal carrier screening was recommended by the American College of Obstetricians and Gynecologists. Demand for other tests, such as fragile X, is also increasing and will probably increase further in the near future.

Quality control (QC) materials, including cell lines, DNA samples and residual patient blood specimens containing characterized mutations detectable by the test methodology and corresponding negative controls are analyzed along with patient specimens to monitor the accuracy of the testing process. These materials are also used to develop and validate new genetic tests. Use of QC materials in patient testing is specified in both regulatory requirements and professional practice guidelines.

Despite the increasing volume and demand for genetic testing as well as professional and regulatory requirements, verified QC materials are not available for many genetic tests, especially tests for disorders with multiple heterogeneous mutations and those for newly defined or rare disorders. Currently testing laboratories and test developers use commercially available cell lines and previously tested patient specimens as QC materials. However, these materials are often unverified and difficult to obtain. The lack of QC material availability also inhibits inter-laboratory comparison of quality and external quality assessment activities.

GOALS of the GTQC Program:

1. Monitor the QC needs of the genetic testing community on a continuing basis

2. Assist the genetic testing community to obtain appropriate and validated materials for quality control, proficiency testing, research, and test development

3. Coordinate contribution, development, validation, and distribution of QC materials for genetic testing.

4. Coordinate information exchange among users, providers and developers of QC materials through an interactive website

5. Sustain a community process for continued QC material development

A Quality Control Material Coordinator (Lisa Kalman, PhD) has been appointed to oversee this program.

The Expert Panel

An expert panel, consisting of representatives from professional organizations, PT/EQA programs, government, research, cell banks, industry and genetic testing laboratories, is available to advise the GTQC Program. This group also helps to prioritize the QC material needs.

GTQC Website

This interactive website facilitates collection of information about community QC needs, disseminates information about the availability of QC materials and solicits involvement of the genetics community in the program.

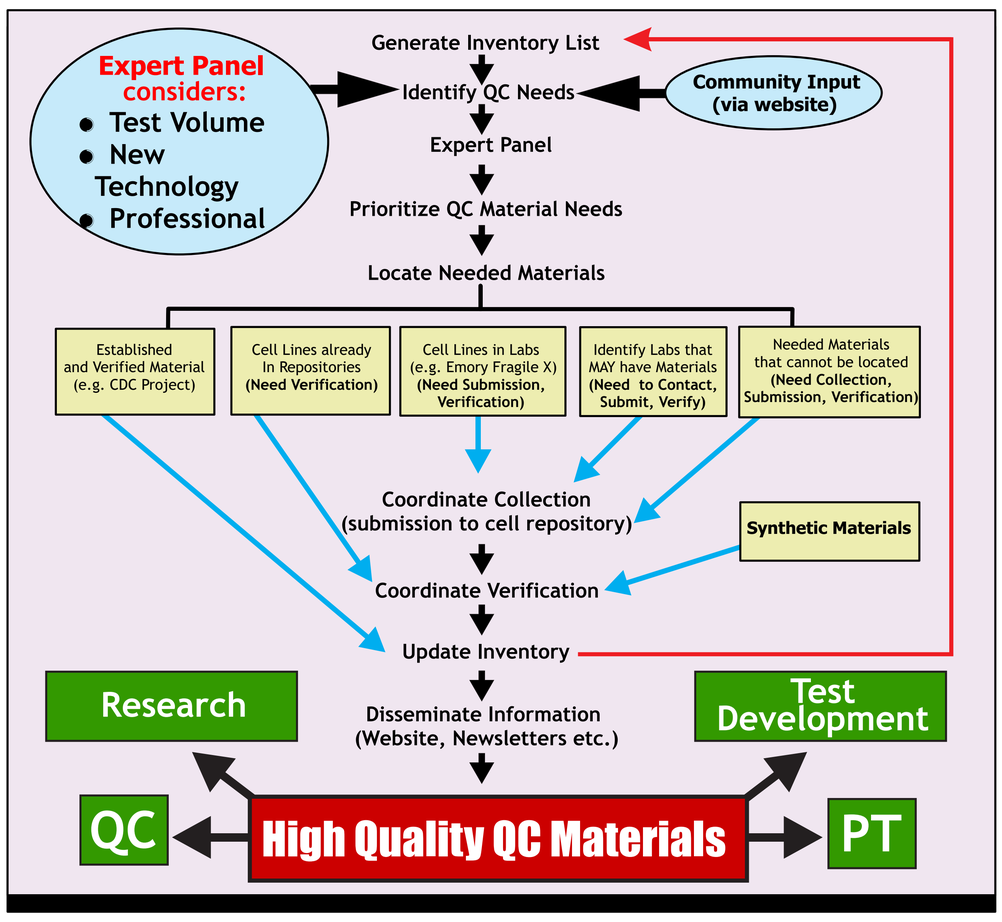
GTQC Homepage-

- Program description
- "Contact us" link- for communication between the genetics testing community and GTQC.

Website Pages-

- **Materials Availability** - Provides tables listing the available QC materials, information about mutations and material type, their source and information about their verification.
- **Needs Monitoring** - Lists QC materials that are needed by the genetic testing community. A "contact us" facilitates communication with the GTQC about QC material needs or potential material contribution.
- **Assistance to Materials Contributors** - Provides information and resources, such as submission and IRB protocols, to assist contributors of QC materials.
- **Reference Articles** - Links to publications and other documents about QC materials
- **Guidance and Oversight** - Links to professional, practice and regulatory guidelines for genetic testing
- **Funding Opportunity and Resource Information** - Links to potential funding sources and incentives offered for material contributors or material testing laboratories

GTQC Flow Chart



Potential Sources of QC Materials

- Cell Repositories
- CRMGEN (a European project to develop certified reference materials)
- National Institute of Standards and Technology
- Biobanks
- Clinical specimens (residual blood and patient recollection)
- Research labs
- Industry/Material developers
- Other?

Current QC Material Availability:

Cystic Fibrosis

- Cell lines containing the 23 mutations on the ACMG CF panel are available as a panel from Coriell Cell Repositories. These mutations have not been verified.
- Verified materials are not available for most other mutations tested in clinical laboratories.
- The GTQC hopes to verify the mutations in the Coriell cell lines by DNA sequence and inter-laboratory analysis.
- Synthetic DNA controls are available for some mutations.

Fragile X

- There are no verified QC materials available for fragile X testing. Most laboratories use previously tested residual blood specimens.
- Certified Reference Materials from the National Institute for Standards and Technology have recently become available for assay calibration, but not routine QC.
- A GTQC fragile X workgroup has identified fragile X QC needs
- Cell lines containing fragile X alleles of interest will be obtained from Coriell Cell Repositories and researchers at Emory University.
- The workgroup is considering validation schemes.

Huntington Disease

- QC needs were identified by consultation with clinical laboratory directors.
- Cell lines are available, and we will begin inter-laboratory verification studies soon.

Ashkenazi Jewish Panel

- Cell lines containing many of the needed mutations for disorders commonly included in Ashkenazi Jewish Panels (Bloom, Canavan, familial Dysautonmia, Gaucher, Niemann-Pick, Tay Sachs and Glycogen Storage diseases) are available from Coriell.
- Inter-laboratory verification studies will begin soon.

Other Disorders

- Many cell lines containing unverified mutations are available from cell repositories
- The CDC, through a contract to Duke University, developed 27 verified cell lines for QC use. These cell lines contain mutations for disorders including cystic fibrosis, Connexin 26, Craniosynostosis/Muenke Syndrome, Hemochromatosis, Huntington Disease, MTHFR and alpha-thalassemia. These cell lines are available from Coriell.

Conclusions

- **QC materials are needed to improve the quality and availability of clinical genetic testing**
- **QC materials are needed for development and assessment of new genetic tests**
- **The Genetic Testing Quality Control Materials Program will work to meet these needs by facilitating development of verified QC materials, fostering communication between users of QC materials, and raising awareness of QC material availability**

Visit our GTQC Website: www.phppo.cdc.gov/dls/genetics/qcmaterials